a=Horizontal distance from point of ascent to a point of a maximum peak height; and
b=Horizontal distance from the point of maximum peak height to point of descent.

The asymmetry factor (A_s) is satisfactory if it is not less than 1.4 and not more than 2.0

(B) *Efficiency of the column.* From the number of theoretical plates (n) calculated as described in §436.216(c)(2) of this chapter calculate the reduced plate height (h_r) as follows:

$$h_r = \frac{(L)(10{,}000)}{(n)(d_p)}$$

where:

L=Length of the column in centimeters;
n=number of theoretical plates; and
d_p=Average diameter of the particles in analytical column packing in micrometers.

The absolute efficiency (h_r) is satisfactory if it is not more than 37.5 for the doxycycline peak.

(C) The resolution (R) between peaks for doxycycline and epi-doxycycline is satisfactory if it is not less than 1.5.

(D) *Coefficient of variation (relative standard deviation).* The coefficient of variation (S_R in percent) of 5 replicate injections is satisfactory if it is not more than 2.0 percent.

(E) *Capacity factor (k′).* Calculate the capacity factor (k') for doxycycline as follows:

$$k' = \frac{t_r - t_o}{t_o}$$

where:

t_r=Retention time of doxycycline in minutes; and
t_o=Column dead time in minutes, which is estimated from the following equation:

$$t_o = \frac{(3.1416)(D^2)(L)(0.75)}{4F}$$

where:

D=Column diameter in centimeters;
L=Column length in centimeters;
0.75=Average total column porosity; and
F=Flow rate in milliliters per minute.

The capacity factor (k') for doxycycline is satisfactory if it is not less than 1.5 and not more than 2.5. If the system suitability requirements have been met, then proceed as described in §436.216(b) of this chapter. Alternate chromatographic conditions are acceptable provided reproducibility and resolution are comparable to the system described. However, the sample preparation described in paragraph (b)(1)(ii)(B) of this section should not be changed.

(iv) *Calculations.* Calculate the doxycycline content as follows:

$$\text{Milligrams of doxycycline per capsule} = \frac{A_u \times P_s \times d}{A_s \times 1{,}000 \times n}$$

where:

A_u=Area of the doxycycline peak in the chromatogram of the sample (at a retention time equal to that observed for the standard);
A_s=Area of the doxycycline peak in the chromatogram of the working standard;
P_s=Doxycycline activity in the doxycycline working standard solution in micrograms per milliliter;
d=Dilution factor of the sample; and
n=Number of capsules in the sample assayed.

(2) *Moisture.* Proceed as directed in §436.201 of this chapter.

(3) *Dissolution.* Proceed as directed in §436.215 of this chapter. The quantity Q (the amount of doxycycline dissolved) is 85 percent at 60 minutes.

(4) *Identity.* The high-pressure liquid chromatogram of the sample determined in paragraph (b)(1) of this section compares qualitatively to that of the doxycycline working standard.

[55 FR 6637, Feb. 26, 1990]

§446.150 Methacycline hydrochloride oral dosage forms.

§446.150a Methacycline hydrochloride capsules.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Methacycline hydrochloride capsules are composed of methacycline hydrochloride and one or more suitable and harmless lubricants and diluents enclosed in a gelatin capsule. Each capsule contains methacycline hydrochloride equivalent to either 70 milligrams of methacycline, 140 milligrams of methacycline, or 280 milligrams of methacycline. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of methacycline that

it is represented to contain. The moisture content is not more than 7.5 percent. The methacycline hydrochloride used conforms to the standards prescribed by § 446.50(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The methacycline hydrochloride used in making the batch for potency, moisture, pH, absorptivity, identity, and crystallinity.

(*b*) The batch for potency and moisture.

(ii) Samples required:

(*a*) The methacycline hydrochloride used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch: A minimum of 30 capsules.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Blend a representative number of capsules in a high-speed glass blender jar containing sufficient sterile distilled water to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.06 microgram of methacycline per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

[39 FR 19076, May 30, 1974, as amended at 43 FR 11163, Mar. 17, 1978; 46 FR 46313, Sept. 18, 1981; 50 FR 19920, May 13, 1985]

§ 446.150b Methacycline hydrochloride oral suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Methacycline hydrochloride oral suspension contains methacycline hydrochloride and one or more suitable and harmless buffers, dispersants, diluents, colorings, flavorings, and preservatives. It contains methacycline hydrochloride equivalent to 14 milligrams of methacycline per milliliter. Its potency is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of methacycline that it is represented to contain. Its pH is not less than 6.5 nor more than 8.0. The methacycline hydrochloride used conforms to the standards prescribed by § 446.50(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The methacycline hydrochloride used in making the batch for potency, moisture, pH, absorptivity, identity, and crystallinity.

(*b*) The batch for potency and pH.

(ii) Samples required.

(*a*) The methacycline hydrochloride used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch: A minimum of 5 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Transfer an accurately measured representative portion of the well-shaken suspension to an appropriate-sized volumetric flask, and dilute to volume with sterile distilled water. Mix well. Remove an aliquot of the stock solution and further dilute with sterile distilled water to the reference concentration of 0.06 microgram of methacycline per milliliter (estimated).

(2) *pH.* Proceed as directed in § 436.202 of this chapter using the undiluted sample.

[39 FR 19076, May 30, 1974, as amended at 43 FR 11163, Mar. 17, 1978; 50 FR 19920, May 13, 1985]

§ 446.160 Minocycline hydrochloride oral dosage forms.

§ 446.160a Minocycline hydrochloride tablets.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Minocycline hydrochloride tablets are composed of minocycline hydrochloride and one or more suitable